

In re Application of:
BARBAS III, et al.
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REMARKS

Regarding the Amendments

Claims 2, 3, 16 and 42 have been amended as set forth in the attached "Version With Markings To Show Changes Made". As amended, the claims are supported by the specification and the original claims. Applicants submit that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Claims 47-50 have been cancelled without prejudice. Thus, upon entry of the amendments, claims 2-5, 16-19, 40 and 42-46 will be pending.

Rejection Under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 42-46 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 10 that claims 42-46 are directed towards a "hybrid" zinc finger protein that binds to a target nucleic acid, the hybrid zinc finger comprising zinc fingers from a first protein linked to zinc fingers from a second protein. The office action alleges that the claims "encompass an enormous genus of possible combinations of zinc finger modules obtained from literally any zinc finger protein."

Applicants do not dispute that the claims encompass a large genus of zinc finger modules obtained from any zinc finger protein. However, the teachings in the specification and in the art provide numerous zinc finger proteins from which to select zinc finger modules for generating a hybrid zinc finger protein as claimed in the present invention. Further, Applicants submit that the specification clearly teaches one of skill in the art how to screen for a zinc finger protein encompassed by claim 42 and claims dependent thereon. For example, the specification teaches that variant/hybrid zinc finger proteins of the invention are useful for suppressing or inducing

gene expression, for example (see page 12, ll. 8-17; page 44, ll. 11-17; pages 46, line 11 through page 51 and the Examples section) and one of skill in the art can use standard gene expression assays to determine whether a particular variant/hybrid zinc finger protein exhibits an effect on expression of a particular gene of interest.

Applicants respectfully disagree with the Examiner's position that there is no description provided wherein "the zinc finger protein variant is a "hybrid" comprising fingers obtained from different types of proteins." Applicants draw the Examiner's attention to page 10, lines 15-25 of the specification, where it states that "A variant may be a hybrid which contains zinc finger domain(s) from one protein linked to zinc finger domain(s) of a second protein, for example." Thus, all of the teaching in the specification relating to "variant" zinc finger proteins also relates to "hybrid" proteins.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 3 and 42-46 under 35 U.S.C. §112, second paragraph. The Examiner's attention is respectfully drawn to the amended claims set forth above.

Claim 3 has been amended to recite that the zinc finger protein is a "variant" of Zif268 or TFIIIA.

Claim 42 has been amended to recite that the hybrid zinc finger protein comprises zinc fingers from a first protein linked to zinc fingers from a second protein *different from the first protein*.

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Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Rejection Under 35 U.S.C. § 102

Applicants respectfully traverse the rejection of claims 2-5 and 16-19 under 35 U.S.C. 102(b) as allegedly anticipated by Hanas et al. Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration (In re Spada, 15 USPQ 2d 1655 (Fed. Cir. 1990), In re Bond, 15 USPQ 2d 1566 (Fed. Cir., 1990). It is respectfully submitted that Hanas et al. does not teach every element of the claimed invention.

The present invention provides variants of zinc fingers wherein the finger modules of the variant have been modified. Applicants teach isolation of modified zinc finger-proteins that bind to a cellular nucleotide sequence different from the cellular nucleotide sequence which it bound prior to modification of the variant. (See application, page 5, lines 23-30, page 43, lines 21-31.) Both the original and modified proteins modulate the function of the cellular nucleotide sequence to which it is bound. Therefore, in modifying the original zinc finger-protein, Applicants teach modification of gene expression.

Hanas et al. describe mutation of TFIIIA by internal deletion, which either eliminates the fourth zinc finger of the protein or results in fusion of the seventh and eighth fingers of TFIIIA. Hanas et al. show that the resulting mutants are capable of promoting 5S gene transcription. (See pages 9864-9865 of Hanas et al.) Hanas et al. do not teach or suggest that the mutated proteins might bind to a different nucleotide sequence thereby potentially serving an additional function in gene expression.

As acknowledged by the Examiner, because claim 40 includes the limitation that “the variant zinc finger polypeptide binds a polynucleotide sequence different from the sequence bound by the “parental” protein...”, claim 40 is deemed to not be anticipated by Hanas et al. Similarly, claims 2 and 16 have been amended to recite this characteristic of the variant polypeptide. Specifically, claims 2 and 16 recite “...wherein said variant binds a polynucleotide sequence different from a sequence bound by a zinc finger-nucleotide binding polypeptide not

having amino acid sequence modification.”.

Accordingly, Hanas et al. does not teach every element of the claimed invention and Applicants respectfully request withdrawal of the rejection of claims 2-5 and 16-19 under 35 U.S.C. 102(b).

Rejection Under 35 U.S.C. §103

The rejection of claims 2, 4, and 16 to 17 under 35 U.S.C. §103(a) as allegedly anticipated by the Crozatier, et al. reference is respectfully traversed.

Crozatier et al. states that “[i]n *vitro* experiments to determine the consequences of the *sry* δ^{F1} , *sry* δ^{F2} , and *sry* δ^4 mutations on the DNA recognition and binding properties of the *sry* δ protein are in progress.” (Crozatier, et al., p. 915, col. 1.) Crozatier et al. do not teach or suggest that the various mutations might be useful for enhancing or repressing gene expression. Even if the teachings of Crozatier motivated one of skill in the art to isolate the mutant peptides of that reference and analyze them for their DNA-binding properties, one would not have had a reasonable expectation of success of obtaining a mutant useful for regulation of gene expression.

As discussed above, the Examiner acknowledged that claim 40 includes the limitation that:

“...the variant zinc finger polypeptide binds a polynucleotide sequence different from the sequence bound by the “parental” protein.” (Paper No. 10, page 4.)

The Examiner has deemed claim 40 to not be anticipated by Hanas et al. Rejection of claim 40 as being obvious over Crozatier has been withdrawn, because claim 40 contains the above limitation. (Paper No. 10, page 5.) Similarly, claims 2 and 16 have been amended to recite this characteristic of the variant polypeptide. Specifically, claims 2 and 16 recite “...wherein said variant binds a polynucleotide sequence different from a sequence bound by a zinc finger-nucleotide binding polypeptide not having amino acid sequence modification.”.

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As such, the claims of the present invention are not obvious in light of the teachings of Crozatier et al. Accordingly, it is respectfully requested that the rejection under 35 U.S.C. §103(a) be removed.

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Double Patenting Rejection

Applicants acknowledge the rejection of claims 2-5, 16-19 and 40 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-7, 21-22, and 53 of U.S. Pat. No. 6,140,466. However, Applicants respectfully defer responding to these rejections until the claims of the subject application are otherwise determined to be in a condition for allowance.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that the pending claims clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

Respectfully submitted,

Date: February 28, 2002

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Attachment A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

2. (Amended) An isolated zinc finger-nucleotide binding polypeptide variant comprising at least two zinc finger modules wherein the amino acid sequence of at least one zinc finger module of said variant has at least one amino acid sequence modification, wherein said variant binds a polynucleotide sequence different from a sequence bound by a zinc finger-nucleotide binding polypeptide not having amino acid sequence modification and wherein the amino acid sequence of each zinc finger molecule that binds a polynucleotide sequence different from a sequence bound by a zinc finger-nucleotide binding polypeptide not having amino acid sequence modification comprises two cysteines and two histidines, whereby both cysteines are amino proximal to both histidines.
3. (Amended) The variant of claim 2, wherein the [which is a] zinc finger-nucleotide binding polypeptide is a variant of a protein selected from [the group consisting of] Zif268 [and] or TFIIIA.
16. (Amended) The isolated zinc finger-nucleotide binding polypeptide variant of claim 2, comprising at least three zinc finger modules wherein at least one module binds to a cellular nucleotide sequence and wherein said variant binds a polynucleotide sequence different from a sequence bound by a zinc finger-nucleotide binding polypeptide not having amino acid sequence modification.
42. (Amended) A hybrid zinc finger protein that binds to a target nucleic acid, the hybrid zinc finger comprising zinc fingers from a first protein linked to zinc fingers from a second protein different from the first protein, wherein the hybrid zinc finger binds a polynucleotide sequence different from a sequence bound by individual modules of the

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first protein and the second protein and wherein the amino acid sequence of each zinc finger protein that binds a target nucleic acid comprises two cysteines and two histidines, whereby both cysteines are amino proximal to both histidines.